

EXPRESS MAIL CERTIFICATE

DOCKET NO.: **176/60088 (6-11406-600)**
APPLICANT: **Howard Federoff**
TITLE: **PRODUCTION OF SOMATIC MOSAICISM IN MAMMALS
USING A RECOMBINATORIAL SUBSTRATE**

Certificate is attached to the **Preliminary Amendment (4 pages) with Appendix A (1 page)** of the above-named application.

EXPRESS MAIL NUMBER: **EL709323334US**
DATE OF DEPOSIT: **May 14, 2001**

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231, Box: Patent Application.

Ruth R. Smith

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Ruth R. Smith

(Signature of person mailing paper
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Howard Federoff)	Examiner:
)	J. Martin
Serial No.	:	Continuation of 08/747,328)	
)	Art Unit:
Cnfrm. No.	:	To Be Assigned)	1632
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Filed	:	Herewith)	
)	
For	:	PRODUCTION OF SOMATIC MOSAICISM IN)	
		MAMMALS USING A RECOMBINATORIAL)	
		SUBSTRATE)	
)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Box: Patent Application

Dear Sir:

Please amend the above-identified application as follows:

In the Specification:

Please cancel the first paragraph on page 1 and insert the following paragraph:

This application is a continuation of U.S. Patent Application Serial
No. 08/747,328, filed November 12, 1996, which claims benefit of U.S. Provisional Patent
Application Serial No. 60/006,622, filed November 13, 1995.

In the Claims:

Please cancel claims 1-66, and add new claims 67-76:

67. (New) A method of activating a gene to be expressed in a
recombinatorial substrate, comprising:

providing a transgenic human carrying a DNA molecule comprising a
recombinatorial substrate, said recombinatorial substrate comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3' to the promoter element to facilitate its transcription;

a terminator positioned 3' to said promoter and 5' to said gene whose expression is to be controlled to prevent transcription of genes 3' to said terminator; and

a first recombination site located 3' to said terminator and a second recombination site located 5' to said terminator, whereby treatment of said DNA molecule with a recombinase specific to the recombination sites removes said terminator from said DNA molecule, thereby activating the recombinatorial substrate and permitting transcription of said gene whose expression is to be controlled, wherein the transgenic human has no gene encoding a recombinase,

introducing into the transgenic human, through its somatic cells, a gene encoding a recombinase and

expressing said recombinase, which when expressed in the somatic cells, will promote the excision of DNA from said first recombination site to said second recombination site within the recombinatorial substrate and wherein activation of said gene whose expression is to be controlled confers a detectable and/or functional phenotype on the human when expressed in the somatic cells of the human.

68. (New) The method of claim 67, wherein said introducing comprises:
providing a vector comprising the gene encoding a recombinase and
introducing the vector directly into the somatic cells of the transgenic human.

69. (New) The method of claim 68, wherein the vector is a virus.

70. (New) The method of claim 69, wherein the virus is selected from the group consisting of adenovirus, adeno-associated virus, lentivirus, vaccinia virus, sinbisvirus, and retrovirus.

71. (New) The method of claim 67, wherein said introducing is carried out by delivering a nucleic acid molecule comprising the gene encoding a recombinase into the somatic cells of the transgenic human by use of virosomes, liposomes, naked DNA, or particle bombardment.

72. (New) The method according to claim 67, wherein the recombinase is selected from the group consisting of FLP and *cre*.

73. (New) A method of activating a recombinatorial substrate, comprising:
providing a transgenic human carrying a DNA molecule comprising a recombinatorial substrate, said recombinatorial substrate comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate,

a gene whose expression is to be controlled, said gene being positioned 3' to the promoter element to facilitate its transcription, and

a first recombination site located 3' to the gene whose expression is to be controlled and a second recombination site located 5' to the gene whose expression is to be controlled, whereby treatment of said DNA molecule with a recombinase specific to the recombination sites removes said gene whose expression is to be controlled from said DNA molecule, thereby activating the recombinatorial substrate and resulting in a loss of function of said gene whose expression is to be controlled, wherein the transgenic human has no gene encoding a recombinase;

introducing into the transgenic human, through its somatic cells, a gene encoding a recombinase, and

expressing said recombinase, which when expressed in the somatic cells, will promote the excision of DNA from said first recombination site to said second recombination site within the recombinatorial substrate and wherein activation of said recombinatorial substrate confers a detectable and/or functional phenotype on the human.

74. (New) The method of claim 73, wherein said introducing comprises:
providing a vector comprising the gene encoding a recombinase;
and

introducing the vector directly into the somatic cells of the transgenic human.

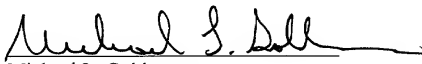
75. (New) The method of claim 74, wherein said introducing is carried out by delivering a nucleic acid molecule comprising the gene encoding a recombinase into the somatic cells of the transgenic human by use of virosomes, liposomes, naked DNA, or particle bombardment.

76. (New) The method of claim 73, wherein the recombinase is selected from the group consisting of FLP and *cre*.

Pursuant to 37 C.F.R. § 1.121, the marked-up version of the above amended paragraph 1, page 1, is appended hereto as Appendix A.

Respectfully submitted,

Date: May 11, 2001


Michael L. Goldman
Registration No. 30,727

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603
Telephone: (716) 263-1304
Facsimile: (716) 263-1600